REMARKS

A. Status of the Claims

Claims 1-3 are currently pending in this application. Claims 1-3 are rejected in the present Office Action. No claims are amended, added, or canceled herein.

B. The Claims are not Obvious under 35 U.S.C. § 103(a).

Claims 1-3 are rejected under 35 USC §103(a) as being obvious over Malfroy-Camine *et al.* (U.S. Patent No. 6,046,188) in view of Crapo *et al.* (U.S. Patent No. 5,994,339) and Winkler *et al.* (Molecular Vision, 1999). According to the Action, "the above references in combination make clear that the claimed compounds are antioxidants having SOD activity"...and "teach a correlation between oxidative damage and macular degeneration and the use of compounds having SOD activity for prevention of such damage." Applicants respectfully traverse.

The Action states on page 3 that Malfroy-Camine *et al.* teach the use of the claimed compounds as antioxidants having superoxide dismutase activity. The Action asserts that Crapo *et al.* teach compounds of similar structure to the claimed compounds for the treatment of disorders such as glaucoma and macular degeneration. The Action also asserts that Winkler *et al.* teach the role of oxidation in relation to macular degeneration and the effect of superoxide dismutase in preventing oxidative damage.

Malfroy-Camine *et al.* do not teach or suggest treatment of macular degeneration, diabetic retinopathy or retinal edema. The teachings of Crapo *et al.* do not remedy this deficiency. Crapo *et al.* relates to a very particular class of SOD mimetics, and teach that the mimetics could be used for the treatment of macular degeneration. The Action asserts that the compounds in Crapo *et al.* are similar to the claimed compounds, which is not the case. The claimed compounds are salen-metal complexes, while the compounds in Crapo *et al.* are

porphyrin-containing compounds. The primary structural similarity of the claimed compounds with the compounds in Crapo *et al.* arises from the manganese ion common to each group of structures. As an infinite number of compounds could use manganese ions as their functional site, this basic similarity is not sufficient to support an inference of motivation. One of skill in the art would not have been motivated to use the lower molecular weight salen-metal complexes for any purpose based on the disclosure and discussion of porphyrin-containing compounds in Crapo *et al.*

In addition, the claimed compounds satisfy one of the objects of the present invention, which is to provide lower molecular weight compounds that catalyze superoxide disproportionation with efficiency comparable to endogenous Mn SOD, while avoiding the bioavailability and immunogenic issues thought to be due to the higher molecular weight species (Spec. page 6, lines 18-25). The lower molecular weight of the claimed compounds has a direct effect on the potential bioavailability improvements, and is an essential component of the uniqueness of the present invention. Thus, the claimed compounds are further distinguished from the compounds of Crapo *et al.*

The Action further asserts that Winkler *et al.* provides the teaching necessary to tie together the compounds of Malfroy-Camine *et al.* with the disclosure in Crapo *et al.*, which teaches that porphyrin-containing SOD mimetics can be used to treat macular degeneration. However, Winkler *et al.* do not actually teach or suggest that compounds with SOD activity can prevent oxidative damage associated with macular degeneration.

Winkler *et al.* is a review paper discussing the role of oxidative damage in the pathology of age-related macular degeneration (AMD). The Action alleges that Winkler *et al.* teach "the effect of superoxide dismutase in preventing oxidative damage," citing the Abstract as support for the assertion. The Abstract states that "actions of antioxidants such as

glutathione, vitamin C, superoxide disumtase, catalase, vitamin E and the carotenoids are discussed in terms of their mechanisms of preventing oxidative damage." In spite of this statement, Winkler *et al.* do not actually discuss the ability of superoxide dismutase, or any antioxidant enzymes, to prevent oxidative damage.

In the paper, Winkler *et al.* merely mention superoxide radical anion as one of a number of oxidants that may play a role in AMD progression (see, for example, figures 2 and 3 on page 34; the last paragraph on page 33; and the second paragraph on page 36). Superoxide dismutase and catalase are identified in the Winkler paper as antioxidant enzymes (see Winkler, page 33), which are only mentioned as part of "the armory of protectants" involved in the reactions that "may be involved in the development of oxidative damage which may lead to AMD." Despite this observation, the paper focuses almost exclusively on studies involving glutathione (GSH), vitamin C, vitamin E, and carotenoids, which are all non-enzyme antioxidants. The paper specifically suggests that carotenoids are predicted to be protective in AMD, and that elevating levels of GSH may be one approach to protect against oxidative damage. Winkler *et al.* never discuss the possibility that mimetics of antioxidant enzymes, or the antioxidant enzymes themselves, could be useful for treating AMD.

The Action asserts that it would have been obvious to combine the teachings of Malfroy-Camine *et al.* with the Winkler paper and Crapo *et al.*, because Malfroy-Camine *et al.* teach the compounds of the invention, while the Winkler paper and Crapo *et al.* allegedly teach that superoxide dismutase compounds can be used to treat macular degeneration. As pointed out above, Crapo *et al.* teach a very specific class of SOD mimetics, which is not similar to the claimed compounds. Thus, the Crapo *et al.* reference, even when read in view of Malfroy-Camine *et al.*, does not render the instant claims obvious. Also, as pointed out above, Winkler *et al.* teach the role of certain non-enzyme antioxidants in protecting against

AMD, but never teach or suggest that mimetics of antioxidant enzymes, such as SOD mimetics, can be used to treat AMD. Consequently, the Winkler *et al.* reference does not stand for the proposition that antioxidant enzyme mimetics are useful for treating AMD. Therefore, the Winkler *et al.* reference, when read in view of Malfroy-Camine *et al.* and Crapo *et al.*, does not render the instant claims obvious.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection be withdrawn.

C. Provisional Double Patenting

Claims 1-3 are provisionally rejected under 35 USC §101 as claiming the same invention as claims 1-3 of copending Application No. 10/729,222. The claims in Application No. 10/729,222 have been amended during prosecution. Thus, the instant claims are not the same as claims 1-3 of copending Application No. 10/729,222. Applicants respectfully request that this rejection be withdrawn.

D. Conclusion

This is submitted to be a complete response to the outstanding Action. The Examiner is invited to contact the undersigned attorney at (817) 615-5330 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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